

## Title (en)

ADENO-ASSOCIATED VIRUS VARIANT CAPSIDS AND USE FOR INHIBITING ANGIOGENESIS

## Title (de)

KAPSID MIT ADENO-ASSOZIIERTEN VIREN VARIANTEN UND VERWENDUNG ZUR HEMMUNG DER ANGIOGENESE

## Title (fr)

CAPSIDES VARIANTES DE VIRUS ADÉNO-ASSOCIÉS ET LEUR UTILISATION POUR INHIBER L'ANGIOGÈNESE

## Publication

**EP 4272728 A2 20231108 (EN)**

## Application

**EP 23186524 A 20181126**

## Priority

- US 201762590976 P 20171127
- US 201862664726 P 20180430
- EP 23152950 A 20181126
- EP 18881166 A 20181126
- US 2018062478 W 20181126

## Abstract (en)

Provided herein are variant adeno-associated virus (AAV) capsid proteins having one or more modifications in amino acid sequence relative to a parental AAV capsid protein, which, when present in an AAV virion, confer increased infectivity of one or more types of retinal cells as compared to the infectivity of the retinal cells by an AAV virion comprising the unmodified parental AAV capsid protein. Also provided are recombinant AAV virions and pharmaceutical compositions thereof comprising a variant AAV capsid protein as described herein, methods of making these rAAV capsid proteins and virions, and methods for using these rAAV capsid proteins and virions in research and in clinical practice, for example in, e.g., the delivery of nucleic acid sequences to one or more cells of the retina for the treatment of retinal disorders and diseases.

## IPC 8 full level

**A61K 9/00** (2006.01)

## CPC (source: EP IL KR US)

**A61K 9/0048** (2013.01 - IL US); **A61K 48/0008** (2013.01 - EP IL KR US); **A61K 48/005** (2013.01 - EP IL KR US);  
**A61K 48/0075** (2013.01 - IL US); **C07K 14/005** (2013.01 - EP IL KR US); **C07K 16/22** (2013.01 - EP IL KR US); **C12N 7/00** (2013.01 - US);  
**C12N 15/86** (2013.01 - EP IL KR); **A61K 9/0048** (2013.01 - EP); **A61K 48/0075** (2013.01 - EP); **C12N 2750/14122** (2013.01 - EP IL KR US);  
**C12N 2750/14143** (2013.01 - EP IL KR US); **C12N 2750/14145** (2013.01 - EP IL KR)

## Citation (applicant)

- WO 2014194132 A1 20141204 - UNIV CALIFORNIA [US]
- US 9193956 B2 20151124 - SCHAFFER DAVID V [US], et al
- US 9186419 B2 20151117 - XIAO XIAO [US], et al
- US 8632764 B2 20140121 - XIAO XIAO [US], et al
- US 8663624 B2 20140304 - SCHAFFER DAVID V [US], et al
- US 8927514 B2 20150106 - CHATTERJEE SASWATI [US], et al
- US 8628966 B2 20140114 - CHATTERJEE SASWATI [US], et al
- US 8263396 B2 20120911 - XIAO WEIDONG [US]
- US 8734809 B2 20140527 - GAO GUANGPING [US], et al
- US 8889641 B2 20141118 - ASOKAN ARAVIND [US], et al
- US 8691948 B2 20140408 - DAVIDSON BEVERLY L [US], et al
- US 8299295 B2 20121030 - MATHARU SAROOP SINGH [US], et al
- US 8802440 B2 20140812 - ZHONG LI [US], et al
- US 8445267 B2 20130521 - ZHONG LI [US], et al
- US 8906307 B2 20141209 - ANDREWS TAE WAN [US], et al
- US 8574583 B2 20131105 - KAY MARK [US], et al
- US 8067015 B2 20111129 - BALABAN NAOMI [US]
- US 7588772 B2 20090915 - KAY MARK [US], et al
- US 7867484 B2 20110111 - SAMULSKI RICHARD JUDE [US], et al
- US 8163543 B2 20120424 - URABE MASASHI [JP], et al
- US 8283151 B2 20121009 - SCHMIDT MICHAEL [US], et al
- US 8999678 B2 20150407 - VANDENBERGHE LUK [US], et al
- US 7892809 B2 20110222 - BOWLES DAWN E [US], et al
- US 7906111 B2 20110315 - WILSON JAMES M [US], et al
- US 7259151 B2 20070821 - ARBETMAN ALEJANDRA ELENA [US], et al
- US 7629322 B2 20091208 - KLEINSCHMIDT JUERGON [DE], et al
- US 7220577 B2 20070522 - ZOLOTUKHIN SERGEI [US]
- US 8802080 B2 20140812 - WARRINGTON KENNETH H [US], et al
- US 7198951 B2 20070403 - GAO GUANGPING [US], et al
- US 8318480 B2 20121127 - GAO GUANGPING [US], et al
- US 8962332 B2 20150224 - GAO GUANGPING [US], et al
- US 7790449 B2 20100907 - GAO GUANGPING [US], et al
- US 7282199 B2 20071016 - GAO GUANGPING [US], et al
- US 8906675 B2 20141209 - GAO GUANGPING [US], et al
- US 8524446 B2 20130903 - GAO GUANGPING [US], et al
- US 7712893 B2 20100511 - DOBASHI HIDETAKA [JP]
- US 6491907 B1 20021210 - RABINOWITZ JOSEPH E [US], et al
- US 8637255 B2 20140128 - WILSON JAMES M [US], et al
- US 7186522 B2 20070306 - LAPEN DANIEL [US], et al
- US 7105345 B2 20060912 - WILSON JAMES M [US], et al
- US 6759237 B1 20040706 - WILSON JAMES M [US], et al
- US 6984517 B1 20060110 - CHIORINI JOHN A [US], et al
- US 6962815 B2 20051108 - BARTLETT JEFFREY S [US]

- US 7749492 B2 20100706 - BARTLETT JEFFREY S [US], et al
- US 6156303 A 20001205 - RUSSELL DAVID W [US], et al
- US 2013295614 A1 20131107 - HAREENDRAN SANGEETHA [IN], et al
- US 2015065562 A1 20150305 - YAZICIOGLU MUSTAFA N [TR], et al
- US 2014364338 A1 20141211 - SCHAFFER DAVID V [US], et al
- US 2013323226 A1 20131205 - WILSON JAMES M [US], et al
- US 2014359799 A1 20141204 - WANG ZHENGNE [US], et al
- US 2013059732 A1 20130307 - LISOWSKI LESZEK [US], et al
- US 2014037585 A1 20140206 - WRIGHT JOHN FRASER [US], et al
- US 2014056854 A1 20140227 - ASOKAN ARAVIND [US], et al
- US 2013296409 A1 20131107 - MILLER ARTHUR DUSTY [US], et al
- US 2014335054 A1 20141113 - GAO GUANGPING [US], et al
- US 2013195801 A1 20130801 - GAO GUANGPING [US], et al
- US 2012070899 A1 20120322 - SHARIFI BEHROOZ [US], et al
- US 2011275529 A1 20111110 - HEILBRONN REGINE [DE]
- US 2011171262 A1 20110714 - BAKKER ANDREW CHRISTIAN [NL], et al
- US 2009215879 A1 20090827 - DIPRIMIO NINA [US], et al
- US 2010297177 A1 20101125 - BUENING HILDEGARD [DE], et al
- US 2010203083 A1 20100812 - LUX KERSTIN [DE], et al
- US 2009317417 A1 20091224 - VANDENBERGHE LUC H [US], et al
- US 2009202490 A1 20090813 - SCHAFFER DAVID V [US], et al
- US 2012220492 A1 20120830 - WEBER THOMAS [US], et al
- US 2006292117 A1 20061228 - LOILER SCOTT A [US], et al
- US 2004002159 A1 20040101 - XIAO WEIDONG [US], et al
- EP 2692731 A1 20140205 - PAUL EHRlich INST BUNDESAMT FUER SERA UND IMPFSTOFFE [DE], et al
- EP 2383346 B1 20141008 - UNIV PENNSYLVANIA [US]
- EP 2359865 B1 20131002 - UNIV PENNSYLVANIA [US]
- EP 2359866 B1 20130717 - UNIV PENNSYLVANIA [US]
- EP 2359867 B1 20141008 - UNIV PENNSYLVANIA [US]
- EP 2357010 B1 20130612 - UNIV PENNSYLVANIA [US]
- EP 1791858 B1 20100421 - INTERCELL AG [AT]
- EP 1668143 B1 20130320 - UNIV PENNSYLVANIA [US]
- EP 1660678 B1 20111026 - UNIV CALIFORNIA [US], et al
- EP 1664314 B1 20081001 - MUELLER DR OLIVER [DE]
- EP 1496944 B1 20080820 - UNIV FLORIDA [US]
- EP 1456383 B1 20140312 - MEDIGENE AG [DE]
- EP 2341068 B1 20130925 - UNIV PENNSYLVANIA [US]
- EP 2338900 B1 20140101 - UNIV PENNSYLVANIA [US]
- EP 1456419 B1 20110817 - UNIV PENNSYLVANIA [US]
- EP 1310571 B1 20060215 - UNIV PENNSYLVANIA [US]
- EP 1633772 B1 20151118 - AVIGEN INC [US]
- EP 1135468 B1 20100106 - UNIV NORTH CAROLINA [US]
- WO 2014124282 A1 20140814 - UNIV PENNSYLVANIA [US]
- WO 2013170078 A1 20131114 - UNIV OREGON HEALTH & SCIENCE [US], et al
- WO 2014160092 A1 20141002 - PHILADELPHIA CHILDREN HOSPITAL [US]
- WO 2014103957 A1 20140703 - TAKARA BIO INC [JP]
- WO 2014052789 A1 20140403 - UNIV NORTH CAROLINA [US]
- WO 2013174760 A1 20131128 - DEUTSCHES KREBSFORSCH [DE]
- WO 2013123503 A1 20130822 - PHILADELPHIA CHILDREN HOSPITAL [US]
- WO 2011038187 A1 20110331 - UNIV PENNSYLVANIA [US], et al
- WO 2008124015 A1 20081016 - UNIV CALIFORNIA [US], et al
- WO 03054197 A2 20030703 - MEDIGENE AG [DE], et al
- WO 0028061 A2 20000518 - UNIV PENNSYLVANIA [US], et al
- WO 9961601 A2 19991202 - US GOV HEALTH & HUMAN SERV [US], et al
- WO 9811244 A2 19980319 - US HEALTH [US], et al
- WO 0044895 A1 20000803 - KREUTZER ROLAND [DE], et al
- WO 9932619 A1 19990701 - CARNEGIE INST OF WASHINGTON [US], et al
- WO 0175164 A2 20011011 - WHITEHEAD BIOMEDICAL INST [US], et al
- WO 0192513 A1 20011206 - JOHNSON & JOHNSON RES PTY LTD [AU], et al
- WO 0129058 A1 20010426 - UNIV MASSACHUSETTS [US], et al
- WO 0189304 A1 20011129 - UNIV ROCHESTER [US], et al
- WO 0216620 A2 20020228 - UNIV SHEFFIELD [GB], et al
- WO 0229858 A2 20020411 - INFINEON TECHNOLOGIES CORP [US]
- US 2004023390 A1 20040205 - DAVIDSON BEVERLY L [US], et al
- US 201313842859 A 20130315
- US 2013032589 W 20130315
- US 2011301073 A1 20111208 - GREGORY PHILIP D [US], et al
- US 7271002 B2 20070918 - KOTIN ROBERT M [US], et al
- US 29795807 F 20071123
- US 2005053922 A1 20050310 - SCHAFFER DAVID V [US], et al
- KOTTERMANSCHAFER, NATURE REVIEW GENETICS, AOP, 20 May 2014 (2014-05-20)
- "GenBank", Database accession no. NC\_002077.1
- SRIVISTAVA ET AL., J. VIROLOGY, vol. 45, 1983, pages 555
- CHIORINI, J. VIROLOGY, vol. 71, 1998, pages 6823
- BANTEL-SCHAAL ET AL., J. VIROLOGY, vol. 73, 1999, pages 3994
- MURAMATSU ET AL., VIROLOGY, vol. 221, 1996, pages 208
- SHADE, J. VIROL., vol. 58, 1986, pages 921
- GAO ET AL., PROC. NAT. ACAD. SCI. USA, vol. 99, 2002, pages 11854
- MORI SWANG LTAKEUCHI TKANDA T: "Two novel adeno-associated viruses from cynomolgus monkey: pseudotyping characterization of capsid protein", VIROLOGY, vol. 330, 2004, pages 375 - 383, XP004676906, DOI: 10.1016/j.virol.2004.10.012
- GRAINGER ET AL., MOL. THER, vol. 11, 2005, pages S337
- ZOLOTUKHIN ET AL., GENE THER, vol. 6, 1999, pages 973
- "Methods in Enzymology", vol. 266, 1996, ACADEMIC PRESS, INC., article "Computer Methods for Macromolecular Sequence Analysis"

- METH. MOL. BIOL., vol. 70, 1997, pages 173 - 187
- J. MOL. BIOL., vol. 48, 1970, pages 443 - 453
- JINEK: "A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity", SCIENCE, vol. 337, no. 6096, 17 August 2012 (2012-08-17), pages 816 - 21, XP055229606, DOI: 10.1126/science.1225829
- QI ET AL.: "Repurposing CRISPR as an RNA-guided platform for sequence-specific control of gene expression", CELL, vol. 152, no. 5, 28 February 2013 (2013-02-28), pages 1173 - 83, XP055346792, DOI: 10.1016/j.cell.2013.02.022
- ASURI ET AL., MOL. THER., vol. 20, no. 2, February 2012 (2012-02-01), pages 329 - 38
- BIBIKOVA ET AL., SCIENCE, vol. 300, no. 5620, 2 May 2003 (2003-05-02), pages 764
- WOOD ET AL., SCIENCE, vol. 333, no. 6040, 15 July 2011 (2011-07-15), pages 307
- OCHIAI ET AL., GENES CELLS, vol. 15, no. 8, August 2010 (2010-08-01), pages 875 - 85
- TAKASU, INSECT BIOCHEM MOL BIOL, vol. 40, no. 10, October 2010 (2010-10-01), pages 759 - 65
- EKKER ET AL., ZEBRAFISH 2008 SUMMER, vol. 5, no. 2, pages 121 - 3
- YOUNG ET AL., PROC NATL ACAD SCI USA., vol. 108, no. 17, 26 April 2011 (2011-04-26), pages 7052 - 7
- GOLDBERG ET AL., CELL, vol. 140, no. 5, 5 March 2010 (2010-03-05), pages 678 - 91
- GEURTS ET AL., SCIENCE, vol. 325, no. 5939, 24 July 2009 (2009-07-24), pages 433
- FLISIKOWSKA ET AL., PLOS ONE, vol. 6, no. 6, 2011, pages e21045
- HAUSCHILD ET AL., PROC NATL ACAD SCI USA., vol. 108, no. 29, 19 July 2011 (2011-07-19), pages 12013 - 7
- YU ET AL., CELL RES, vol. 21, no. 1, November 2011 (2011-11-01), pages 1638 - 40
- HOCKEMEYER ET AL., NAT BIOTECHNOL., vol. 29, no. 8, 7 July 2011 (2011-07-07), pages 731 - 4
- TESSON ET AL., NAT BIOTECHNOL., vol. 29, no. 8, 5 August 2011 (2011-08-05), pages 699 - 700
- KOERBER, J. T. ET AL., HUM. GENE THER., vol. 18, 2007, pages 367 - 378
- GAO G-PALVIRA MRWANG LCALEDJO RJOHNSTON JWILSON JM: "Novel adeno-associated viruses from rhesus monkeys as vectors for human gene therapy", PROC NATL ACAD SCI U S A, vol. 99, 2002, pages 11854 - 9
- ATCHISON RWCASTO BCHAMMON WM, SCIENCE, vol. 149, 1965, pages 754 - 6
- HOGGAN MDBLACKLOW NRROWE WP: "Studies of small DNA viruses found in various adenovirus preparations: physical, biological, and immunological characteristics", PROC NATL ACAD SCI U S A, vol. 55, 1966, pages 1467 - 74
- BLACKLOW NRHOGGAN MDROWE WP: "Isolation of adenovirus-associated viruses from man", PROC NATL ACAD SCI U S A, vol. 58, 1967, pages 1410 - 5
- BANTEL-SCHAAL UZUR HAUSEN H: "Characterization of the DNA of a defective human parvovirus isolated from a genital site", VIROLOGY, vol. 134, 1984, pages 52 - 63, XP023049543, DOI: 10.1016/0042-6822(84)90271-X
- MAYOR HDMELNICK JL: "Small deoxyribonucleic acid-containing viruses (picodnavirus group)", NATURE, vol. 210, 1966, pages 331 - 2
- FLOTTE TR: "Gene therapy progress and prospects: recombinant adeno-associated virus (rAAV) vectors", GENE THER., vol. 11, 2004, pages 805 - 10, XP037770456, DOI: 10.1038/sj.gt.3302233
- LODERIO ET AL., PNAS, vol. 109, no. 17, 2012, pages 6513 - 6518
- BOWLES, D ET AL., J. VIROL., vol. 77, 2003, pages 423 - 432
- GRAY ET AL., MOL. THER., vol. 18, 2010, pages 570 - 578
- GRIMM, D. ET AL., J. VIROL., vol. 82, pages 5887 - 5911
- KOERBER, J. T. ET AL., MOL. THER., vol. 16, 2008, pages 1703 - 1709
- LI W ET AL., MOL. THER., vol. 16, 2008, pages 1252 - 1260
- KOERBER, J. T. ET AL., METHODS MOL. BIOL., vol. 434, 2008, pages 161 - 170
- KOERBER, J. T. ET AL., MOL. THER., vol. 17, 2009, pages 2088 - 2095
- MAHESHRI, N ET AL., NATURE BIOTECH, vol. 24, 2006, pages 198 - 204
- DALKARA, D. ET AL., SCI. TRANSL. MED., vol. 5, 2013, pages 189ra76
- LISOWSKI, L. ET AL., NATURE, vol. 506, 2013, pages 382 - 286
- YANG, L. ET AL., PNAS, vol. 106, 2009, pages 3946 - 3951
- GAO, G ET AL., MOL. THER., vol. 14, 2006, pages 809 - 87
- BELL, P. ET AL., HUM. GENE THER., vol. 22, 2011, pages 985 - 997
- PADRON, J. VIROL, vol. 79, 2005, pages 5047
- SHEN ET AL., MOL. THER., vol. 15, 2007, pages 1955
- LI ET AL., NATURE, vol. 475, 2011, pages 217
- STINSKI ET AL., JOURNAL OF VIROLOGY, vol. 55, no. 2, 1985, pages 431 - 441
- MIYAZAKI ET AL., GENE, vol. 79, no. 2, 1989, pages 269 - 277
- JACOBSON ET AL., MOLECULAR THERAPY, vol. 13, no. 6, 2006, pages 1074 - 1084
- KIM, GENE, vol. 91, no. 2, 1990, pages 217 - 223
- SINGER-SAM ET AL., GENE, vol. 32, no. 3, 1984, pages 409 - 417
- WULFF, FEBS LETTERS, vol. 261, 1990, pages 101 - 105
- YOUNG ET AL., OPHTHALMOL. VIS. SCI., vol. 44, 2003, pages 4076
- NICLOUD ET AL., J. GENE MED, vol. 9, 2007, pages 1015
- YOKOYAMA, EXP EYE RES, vol. 55, 1992, pages 225
- TUCKER ET AL., PNAS, vol. 91, 1994, pages 2611 - 2615
- PARK ET AL., GENE THERAPY, vol. 16, no. 7, 2009, pages 916 - 926
- FURUKAWA ET AL., THE JOURNAL OF NEUROSCIENCE, vol. 22, no. 5, 2002, pages 1640 - 1647
- LEE ET AL., GENE THERAPY, vol. 17, 2010, pages 1390 - 1399
- AKIMOTO ET AL., PNAS, vol. 103, no. 10, 2006, pages 3890 - 3895
- LI ET AL., BIOCHEMISTRY AND MOLECULAR BIOLOGY, vol. 43, 2002, pages 1375 - 1383
- YE ET AL., HUMAN GENE THERAPY, vol. 27, no. 1, 2016, pages 72 - 82
- MEUR ET AL., GENE THERAPY, vol. 14, 2007, pages 292 - 303
- KENNEDY ET AL., JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, 1998, pages 5591 - 5598
- KOJIMA ET AL., MOLECULAR AND CELLULAR BIOCHEMISTRY, vol. 293, no. 1-2, 2006, pages 63 - 69
- ESUMI ET AL., THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 279, no. 18, 2004, pages 19064 - 19073
- BESNARD ET AL., JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 266, no. 28, 1991, pages 18877 - 18883
- CRONIN ET AL., EMBO MOLECULAR MEDICINE, vol. 6, no. 9, 2014, pages 1175 - 1190
- A. GENNARO: "Remington: The Science and Practice of Pharmacy", 2000, LIPPINCOTT, WILLIAMS, & WILKINS, article "Amer. Pharmaceutical Assoc"
- "Pharmaceutical Dosage Forms and Drug Delivery Systems", 1999, LIPPINCOTT, WILLIAMS, & WILKINS
- SAMBROOK ET AL.: "Molecular Cloning: A Laboratory Manual", 2001, HARBOR LABORATORY PRESS
- BOLLAG ET AL.: "Protein Methods", 1996, JOHN WILEY & SONS
- "Viral Vectors", 1995, ACADEMIC PRESS
- "Immunology Methods Manual", 1997, ACADEMIC PRESS
- DOYLEGRIFITHS: "Cell and Tissue Culture: Laboratory Procedures in Biotechnology", 1998, JOHN WILEY & SONS

AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

DOCDB simple family (publication)

**WO 2019104279 A1 20190531**; AU 2018372235 A1 20200611; AU 2018372235 B2 20220224; AU 2018372235 B9 20220310; AU 2022203494 A1 20220609; AU 2022203494 B2 20240801; BR 112020010674 A2 20201110; CA 3083472 A1 20190531; CL 2020001360 A1 20200911; CN 111770999 A 20201013; CR 20200282 A 20210218; DK 3717636 T3 20230530; DK 3717636 T5 20240826; EP 3717636 A1 20201007; EP 3717636 A4 20210908; EP 3717636 B1 20230308; EP 4219695 A2 20230802; EP 4219695 A3 20240117; EP 4272728 A2 20231108; EP 4272728 A3 20240612; ES 2946747 T3 20230725; FI 3717636 T3 20230601; IL 274712 A 20200730; JP 2021503914 A 20210215; JP 2022121534 A 20220819; JP 2024015194 A 20240201; JP 7184894 B2 20221206; KR 20200088853 A 20200723; MX 2020005451 A 20200827; NZ 765038 A 20240830; PE 20210915 A1 20210519; PH 12020550706 A1 20210426; PT 3717636 T 20230530; RU 2020121215 A 20211229; RU 2020121215 A3 20211229; SG 11202004545X A 20200629; UA 127831 C2 20240117; US 11766489 B2 20230926; US 2020282077 A1 20200910

DOCDB simple family (application)

**US 2018062478 W 20181126**; AU 2018372235 A 20181126; AU 2022203494 A 20220523; BR 112020010674 A 20181126; CA 3083472 A 20181126; CL 2020001360 A 20200522; CN 201880087687 A 20181126; CR 20200282 A 20181126; DK 18881166 T 20181126; EP 18881166 A 20181126; EP 23152950 A 20181126; EP 23186524 A 20181126; ES 18881166 T 20181126; FI 18881166 T 20181126; IL 27471220 A 20200517; JP 2020528888 A 20181126; JP 2022101767 A 20220624; JP 2023205214 A 20231205; KR 20207017143 A 20181126; MX 2020005451 A 20181126; NZ 76503818 A 20181126; PE 2020000575 A 20181126; PH 12020550706 A 20200526; PT 18881166 T 20181126; RU 2020121215 A 20181126; SG 11202004545X A 20181126; UA A202003841 A 20181126; US 201816765758 A 20181126